

REMARKS

Claims 1-24, 28-39 and 151 are pending in this application. Claims 25-27 and 40-150, having been previously withdrawn as directed to non-elected subject matter, have been canceled without prejudice to Applicants' rights to prosecute any subject matter not claimed by the instant application in any number of continuation or divisional applications.

Claims 2 and 3 have been amended, to more particularly specify “the first polymer sequence” rather than “a particular polymer sequence” of the independent claim. Similarly, Claim 5 has been amended to depend from claim 4. Claim 19 has been amended to recite “the plurality of biopolymers” as opposed to “the biopolymer.” Finally, Claim 24 has been amended to recite the steps of:

“ligating the identified biopolymer fragment to the parent fragment, if the identified biopolymer fragment has an identified possible cut-point at the end of the fragment; and

repeating the randomly identifying step and the ligating step until the data structure, representing the crossover mutant is the desired length.”

Support for these amendments can be found throughout the specification and in the claims as originally filed. Hence, no new matter has been introduced with these amendments. Entry of the above amendments is therefore respectfully requested.

The Examiner's Objections

The Examiner objected to the title of the invention as allegedly not descriptive. Accordingly, Applicants have amended the title to read “METHODS AND SYSTEMS FOR CALCULATING THE CROSSOVER POINT FOR BIOPOLYMER CREATION.” Applicants respectfully submit the title is now in a form that complies with the guidelines.

The Examiner objected to the abstract of the invention as allegedly not giving the steps of the process claims. Accordingly, Applicants have amended the abstract of the invention to read "Specifically, the methods of the invention include analytical methods for identifying "crossover locations" in a polymer by identifying coupling interactions between residues; generating a plurality

The Rejections For Obviousness Under 35 U.S.C. §103

Claims 1-18, 23-33, 36-37, 40 and 151 have been rejected as obvious over Bogarad *et al* *Proc. Natl. Acad. Sci.* 96, 2591-2595, 1999 (“Bogarad”) in view of Panchenko *et al*. *Proc. Natl. Acad. Sci.* 93, 2008-2013, 1996 (“Panchenko”)

In order to properly determine a prima facie case of obviousness, an examiner “must step backward in time and into the shoes worn by the hypothetical ‘person of ordinary skill in the art’ when the invention was unknown and just before it was made.” M.P.E.P. § 2142. This is important, as “impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.” *Id.* Three basic criteria must then be met: first, there must be some suggestion or motivation to modify or combine the cited references; second, there must be a reasonable expectation of success; and third, the prior art references must teach or suggest all the claim limitations. *Id.* at § 2143. With regard to the first criterion, it is important to recognize that the “mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.” *Id.* at § 2143.01 (citing *In re Mills*, 916 F.3d 680 (Fed. Cir. 1990)).

Claims 1-18, 23-33, 36-37, 40 and 151 relate, *inter alia*, to methods and computer systems for selecting a crossover location in a plurality of biopolymer sequences for recombination. Bogarad allegedly relates to a method for protein or nucleic acid molecular evolution by recombination or mutagenesis. The examiner alleges that the method of Bogarad utilizes an energy function as the selection criteria for identifying optimal sequences which includes secondary structure subdomain energies and subdomain-subdomain interaction energies. The examiner admits that Bogarad does “not explicitly teach how the sites or locations of the domains or structures for swapping/recombination... are selected.” (Page 6).

While Bogarad does describe a method of modeling the molecular evolution of protein sequences, Brogard does not teach or suggest Applicants' claimed method for selecting a crossover location in a plurality of biopolymer sequences for recombination. Borarad describes "the combination of DNA shuffling with synthetic splicing libraries that contain representative pools of

native low energy structures encoded within multiple short exons” (p. 2593) and utilizing these synthetic oligonucleotide pools to “make the assembly, shuffling and swapping steps possible.” (P. 2594). Bogarad does not determine the crossover location by alignment of a plurality of biopolymers prior to recombination but instead utilizes a library of exon pools to make an array of sequences and utilizes an energy function to determine which combination of pool exons has the lowest evolved energy after shuffling and swapping of codons.

Panchenko does nothing to rectify the deficiencies of Bogarad. Panchenko allegedly discloses a computer algorithm for identifying the boundaries of foldon structures in a protein sequence. Through the measurement of relative foldability one residue at a time, Panchenko can determine the boundaries of the folding regions for a particular protein. The foldon interactions are determined only for a single protein within itself. Nowhere does Panchenko describe the foldon interactions between a plurality of biopolymers. Even if one were to assume that Panchenko could determine the location for an ideal mutation on one biopolymer, Panchenko is silent as to determining the location of a crossover mutation between two or more biopolymers based on the interactions between the two biopolymers.

The Examiner has not demonstrated that Bogarad in combination with Panchenko suggests a method for determining the location for a crossover mutation between two or more biopolymers based on the interaction energies between the biopolymers. In addition, the Examiner has not demonstrated that it would have provided those of ordinary skill in the art with a reasonable expectation of successfully obtaining the claimed invention. *In re Fine* 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988).

The Examiner has further rejected Claims 19-24, 34-35 and 38-39 as obvious over Bogarad in view of Panchenko and Jonsson *et al Nucleic Acids Research* 21, 733-739, 1993 (“Jonsson”).

Jonsson does nothing to rectify the deficiencies of Bogarad and Panchenko described above. Jonsson utilizes quantitative sequence-activity monitoring *in silico* to determine for each group of descriptors for each position has a preferred energy through partial least squares projections to latent structures (p. 736) Jonsson does not determine the location of cutpoints for a crossover

mutation between a plurality of biopolymers but instead looks at each base separately and determines which base out of the group represents the lowest energy from a matrix and generates a synthetic sequence base by base.

As the art cited by the examiner in no way teaches or suggests all the claim limitations and provides no reasonable expectation of success, Applicants respectfully submit that the claims are not obvious over Bogarad, Panchenko and/or Jonsson alone or in combination and request the withdrawal of the rejection.

The Rejections for Provisional Statutory-type Double Patenting:

Claims 1-24, 28-40 and 151 have also been provisionally rejected under 35 U.S.C. § 101. In particular, the Examiner argues that these claims are identical to the claims in copending U.S. Application No. 10/016,668 (“the ‘668 application”). Applicants agree to cancel Claims 1-24, 28-40 and 151 in the copending ‘668 application. Upon such cancellation, this rejection will be obviated.

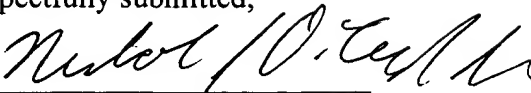
Conclusions:

For the reasons set forth above, Applicants believe that each of the Examiner’s objections to this application and rejections of the pending claims have been overcome and/or obviated.

Accordingly, the withdrawal of all objections and rejections and the reconsideration of this application are respectfully requested. An allowance is earnestly sought.

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Respectfully submitted,

By 

Nicholas J. DiCeglie, Jr.

Registration No.: 51,615

DARBY & DARBY P.C.

P.O. Box 5257

New York, New York 10150-5257

(212) 527-7700

(212) 753-6237 (Fax)

Attorneys/Agents For Applicant